## REMARKS

By this amendment, Claims 1, 2, 5, 6, 24 and 32 have been amended. Claims 7-19, 25-31 and 33-37 have been canceled without prejudice to refiling in continuing applications. New claims 38-42 have been added which recite a method for deleting a nucleic acid from a cell that is part of a tissue and the regulatable promoter is a promoter specifically expressed in said tissue. It is believed that none of the amendments constitute new matter.

*Claim Rejections – 35 U.S.C. §112, First Paragraph*

The Examiner has maintained a rejection of all of the claims presently under examination (*i.e.*, 1-17, 19-35 and 37) under 35 U.S.C. §112, first paragraph, for lack of enablement. The Examiner is of the opinion that while the specification is enabling for a method for deleting a nucleic acid sequence in a specified tissue in a mouse, the specification does not enable such methods for other organisms. The essence of the Examiner's enablement rejections appears to be that the specification has not shown the introduction of DNA into embryonic stem cells for other than mice and that such methods are unpredictable. The Examiner has interpreted language in the claims which recites introducing DNA into an organism as encompassing the use of stem cells and transgenic animals from other than mice. Accordingly, the Examiner is of the opinion that manipulation of stem cells and generation of transgenic animals is an unpredictable endeavor that is not enabled by the specification for any animal other than a mouse.

The claims have been amended to recite a method for deleting a nucleic acid sequence from a DNA molecule that has been introduced into a cell, whereby the sequence is deleted in a regulatable manner utilizing a regulatable promoter. Support for this amendment can be found, *inter alia*, at page 6, Table 1, which demonstrated specific excision of the ACN gene in germline cells of transgenic mice utilizing a spermatogenesis-specific promoter to regulate expression of the Cre recombinase.

The Examiner is further of the opinion that some of the claims are directed to gene therapy (claims 32, 33 and 34) or use in gene therapy (claim 6) and thus are not enabled, since it is well known that the state of art of gene therapy is undeveloped and unpredictable in achieving *in vivo* therapeutic expression levels of a gene of interest. The relevant claims have been amended or

otherwise canceled to recite molecules or methods for deleting a nucleic acid of interest from a cell, wherein the deleted nucleic acid comprises a wild-type allele or fragment thereof of a gene. The specification clearly shows how to make and use the presently claimed invention, including the presentation of experimental details and results. Applicants would also reiterate that it is not necessary to introduce the DNA constructs into embryonic stem cells for the invention to work. That is, Applicants are not creating transgenic animals. It is submitted that the Examiner has not provided any sound reasons why the presently claimed invention would not be enabled to a skilled artisan.

In view of the amendments to the claims and above arguments, it is believed that the pending claims satisfy the provisions of the applicable statutes and withdrawal of the rejections under 35 U.S.C. 112, first paragraph for lack of enablement is requested.

The Examiner has not specified an independent basis for rejecting claim 20 and the claims which depend therefrom for lack of enablement. Claim 20 recites a nucleic acid molecule comprising a recombinase site, a tissue specific promoter, a recombinase gene, foreign DNA and another recombinase site. A nucleic acid molecule as in claim 20 has been described in the specification. Furthermore, as noted by the Examiner at page 3, the specification is enabling for a method for deleting a nucleic acid utilizing a nucleic acid molecule as in claim 20. It is thus submitted that claim 20 and the claims which depend therefrom are enabled and withdrawal of this ground of rejection is requested.

## CONCLUSION

In view of the above amendments and remarks, it is believed that the present application satisfies the provisions of the patent statutes and the pending claims are patentable over the cited prior art. Reconsideration of this application and early notice of allowance are requested. The

Examiner is invited to telephone the undersigned if it will help expedite the allowance of the application.

| RESPECTFULLY SUBMITTED, | | | | | |
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**Attachments**: **Version with markings to show changes made**

**Amended Claims : Version with markings to show changes made**

1. (Twice Amended) A method for deleting a nucleic acid sequence from a DNA molecule that has been introduced into [an organism] an animal cell, whereby said sequence is deleted in a [tissue-specific] regulatable manner utilizing a regulatable promoter, said DNA molecule comprising a recombinase site, a [tissue-specific] regulatable promoter, a recombinase gene, a foreign DNA and a recombinase site, the method comprising growing said [organism] cell such that the [tissue-specific] regulatable promoter is active, said recombinase gene is expressed in the specified tissue and said foreign DNA is deleted.

2. (Amended) The method of claim 1, wherein the DNA molecule further comprises a gene which is desired to be expressed in the [organism] cell.

5. (Amended) The method of claim 1, wherein said foreign DNA is a wild-type allele or fragment thereof of a gene[ for use in gene therapy].

6. (Amended) The method of claim 2, wherein said foreign DNA is a wild-type allele or fragment thereof of a gene[ for use in gene therapy].

24. (Twice Amended) The molecule of claim 20, wherein said molecule further comprises a gene which is desired to be expressed in [an organism] a cell.

32. (Twice Amended) The method of claim 20, wherein said foreign DNA is a wild-type allele or fragment thereof of a gene[ for use in gene therapy].